Office Action Summary	Application No.	Applicant(s)
	10/597,545	JENSEN ET AL.
	Examiner	Art Unit
	JODY KAROL	1627

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *11 May 2011*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,3-20 and 23-28* is/are pending in the application.

4a) Of the above claim(s) *5-7,9 and 24-26* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1, 3, 4, 8, 10-20, 23, 27, and 28* is/are rejected.

7)☒ Claim(s) *27* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Applicant's response to the Election/Restriction Requirement filed on 5/11/2011 has been received and entered into the Application. Claims 1, 3-20, and 23-28 are pending.

Election/Restrictions

1. Applicant's election without traverse of Group II, claims 1, 2-30, 23, 24, 27, and 28, directed methods of reduction of the visible signs of fine lines on the skin in an individual in need thereof comprising contacting the skin of said individual with a composition comprising at least one ACD inhibitor and/or angiotensin receptor antagonist and the species election without traverse of captopril as the ACE inhibitor and losartan as the angiotensin II receptor antagonist in the reply filed on 5/111/2011 is acknowledged.

Claims 5-7, 9, and 24-26 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Accordingly, claims 1, 3, 4, 8, 10-20, 23, 27, and 28 are examined on the merits herein, and prior art is applied in so much as it reads on the elected species.

WITHDRAWN REJECTIONS

2. In view of the elections of species requirement and Applicant's cancellation of claim 2, the rejection of claims 2, 5-7, and 9 under 35 U.S.C. 112, 1st paragraph, for lack of full enablement, is herein withdrawn.

3. In view of Applicant's amendment to claim 1 and cancellation of claims 2, the rejection of claims 1-4, 12-16, and 18 under 35 U.S.C. 102(b) as anticipated by Alert et al. (US 5,728,373) moot. Thus, said rejection is herein withdrawn.

4. In view of the election of species requirement and the cancellation of claim 2, the rejection of claims 1-5, 11-16, 18, and 20 under 35 U.S.C. 102(e) as being anticipated by Linter (US 2005/0142092 A1) is herein withdrawn.

5. In view of the election of species requirement and the cancellation of claim 2, the rejection of claims 1-7, 9, 12, and 14 under 35 U.S.C. 102(e) as being anticipated by Li et al. (US 6,805,878 B2) is herein withdrawn.

6. In view of the election of species requirement, the rejection of claims 10 and 19 under 35 U.S.C. 103(a) as being unpatentable over Linter (US 2005/0142092 A1) is herein withdrawn.

REJECTIONS

7. The following rejections and/or objections are either maintained from the previous Office Action dated 5/25/2010 or newly applied. They constitute the complete set of rejections and/or objections presently being applied in the instant application. The newly applied rejections are necessitated by the species election, the amendment of claims 1, 16 and 17, and the addition of new claims 23, 27, and 28.

Claim Objections

Claim 27 is objected to because of the following informalities: Claim 27 recites duplicates of several of the ACE inhibitors and angiotensin II receptor antagonists (i.e. fosinipril, losartan, etc.). Appropriate correction is required.

Claim Rejections - 35 USC § 112

Second Paragraph Rejection

8. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 27 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 27 contains the trademark/trade names Cozaar®, Diovan®, Avapro®, Atacand®, and Micardis®. Where a trademark or trade name is used in a claim as a limitation to identify or describe a particular material or product, the claim does not comply with the requirements of 35 U.S.C. 112, second

paragraph. See *Ex parte Simpson*, 218 USPQ 1020 (Bd. App. 1982). The claim scope is uncertain since the trademark or trade name cannot be used properly to identify any particular material or product. A trademark or trade name is used to identify a source of goods, and not the goods themselves. Thus, a trademark or trade name does not identify or describe the goods associated with the trademark or trade name. In the present case, the trademark/trade name is used to identify/describe losartan, valsartan, irbesartan, candesartan, and telmisartan, accordingly, the identification/description is indefinite.

Scope of Enablement Rejection

9. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

10. Claims 1, 3, 4, 8, 10-20, 23 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a cosmetic method for reduction of the visible fine lines on the skin in an individual in need thereof, comprising administering a composition comprising captopril, a pharmaceutically acceptable salt thereof, or a compound as listed in claims 27-28, does not reasonably provide enablement for a cosmetic method for improving aspects of an individual's skin tone including methods for the treatment of skin aging or wrinkling comprising administering at least one of each and every ACE inhibitor, each and every angiotensin II receptor antagonist, or each and every combination thereof. The specification does not enable any person skilled in the

art to which it pertains, or with which it is most nearly connected, to make or use the invention commensurate in scope with these claims.

The test of enablement is whether one skilled in the art could make and use the claimed invention from the disclosures in the application coupled with information known in the art without **undue experimentation** *(United States v. Telectronics, Inc.,* 8 USPQ2d 1217 (Fed. Cir. 1988). Whether undue experimentation is required is not based upon a single factor, but rather is a conclusion reached by weighing many factors. These factors were outlined in *Ex parte Forman,* 230 USPQ 546 (Bd. Pat. App. & Inter. 1986) and again in *In re Wands,* 8 USPQ2d 1400 (Fed. Cir. 1988) and include the following: (1) breadth of the claims; (2) nature of the invention; (3) state of the prior art; (4) amount of direction provided by the inventor; (5) the level of predictability in the art; (6) the existence of working examples; (7) quantity of experimentation needed to make or use the invention based on the content of the disclosure; and (8) relative skill in the art. All of the factors have been considered with regard to the claims, with the most relevant factors discussed below:

(1) The nature of the invention: The instant invention pertains to cosmetic methods of improving aspects of an individual's skin tone comprising contacting the skin with a composition comprising at least one of any ACE inhibitor, any angiotensin II receptor antagonist, or combinations thereof and methods of treatment of skin aging or wrinkling comprising administering of any ACE inhibitor, any angiotensin II receptor antagonist, or combinations thereof to an individual in need thereof.

(2) The breadth of claims: Claims 1, 3, 4, 8, 10-14, 27, and 28 are directed to methods of reducing the visible signs of fine lines in the skin in an individual in need thereof, comprising contacting the skin with a composition comprising at least one of any ACE inhibitor, any angiotensin II receptor antagonist, or combinations thereof. Claims 15, 16, and 18-20 are directed to methods of treatment of wrinkling comprising administering of any ACE inhibitor, any angiotensin II receptor antagonist, or combinations thereof to an individual in need thereof. The treatment with any ACE inhibitor, any angiotensin II receptor antagonist, or combinations thereof encompasses treatment with a large number of compounds that may or may not yet be known, which is not supported by the instant specification.

(3) The state of the prior art: It is known in the art to treat the aging or damaged skin with certain ACE inhibitors. For example, Alert et al. teach the treatment of UV-induced skin damage with compositions containing captopril (see US 5,728,373 - cited on IDS). Further, Lintner et al. (teach the treatment of bags and circles under the eyes, visible signs of ageing and fatigue, by administering a composition comprising ACE enzyme inhibitor dipeptides (see US 2005/0142092 A1 - cited on IDS). However, there is no evidence in the prior art that administering each and every ACE inhibitor, each and every angiotensin II receptor antagonists, or combinations thereof in general, would reduce the visible signs of fine lines on the skin or treat wrinkles. Moreover, the instant specification specifically states that the "ACE and angiotensin II are known to be involved in triggering collagen synthesis, whereas teaching with the prior art

suggest that aging skin is associated with the reduction collagen" and states that it is surprising and unexpected that the inhibitors and antagonists of said enzymes do not lead to damaging levels of skin collagen production but improve and/or maintain the skin tone of an individual (see page 5 of the instant specification, lines 5-16). Thus, the state of the prior art at the time of the instant invention is that ACE inhibitors and angiotensin II antagonists were not known to improve aspects of an individual's skin tone, treat skin aging, or treat wrinkles.

(4) The amount of direction provided by the inventor: There is nothing in the specification that would indicate that the current invention is able to reduce the visible signs of fine lines on the skin, or treat wrinkles with each and every ACE inhibitor, each and every angiotensin II antagonist, or combinations thereof. A list of numerous examples of ACE inhibitors and angiotensin II antagonists are provided on page 5, lines 26 to page 8, line 21 of the instant specification. General guidance for the dosage, administration, and formulation of cosmetic formulations, including acceptable cosmetic auxiliaries is provided on page 8, line 24 to page 33, line 20 of the instant specification.

(5) Predictability of the art: The prior art does not teach that each and every ACE inhibitor known or not yet discovered, each and every, angiotensin II receptor antagonist known or not yet discovered, or combinations thereof will reduce the visible signs of fine lines on the skin, or treat wrinkles. Although captopril and ACE enzyme inhibitor dipeptides are known to treat some aspects of skin aging, the instant specification states that it is expected that ACE inhibitor, angiotensin II receptor antagonist, or combinations thereof would decrease skin

collagen, wherein skin aging is already associated with a reduction in skin collagen. Thus, there is little predictability in the art regarding the will reduction of the visible signs of fine lines on the skin or the treatment of wrinkles with each and every ACE inhibitor known or not yet discovered, each and every, angiotensin II receptor antagonist known or not yet discovered, or combinations thereof.

(6) The presence or absence of working examples: Applicant describes a formulation example of pages 34-36 of the instant specification and prophetic example for the topical application of ACE inhibitors on pages 36-38. However, the Applicant does not supply any concrete evidence that topical application of each and every ACE inhibitor known or not yet discovered, each and every, angiotensin II receptor antagonist known or not yet discovered, or combinations thereof will reduce the visible signs of fine lines on the skin or treat wrinkles.

Overall, applicant fails to provide examples indicating that the instant method can reduce the visible signs of fine lines on the skin or treat wrinkles. Therefore, the practitioner would turn to trial and error experimentation to make/use the instant compositions for reducing the visible signs of fine lines on the skin or treating wrinkles, without guidance from the specification or the prior art.

(7) The quantity of experimentation: In order to utilize the methods as claimed, the skilled artisan would be presented with an unpredictable amount of experimentation to determine, for example, which ACE inhibitors, angiotensin II receptor antagonists, or combinations thereof were effective reducing the visible

signs of fine lines on the skin or treating wrinkles, and effective dosages for each treatment. The number of ACE inhibitors and angiotensin II receptor antagonists known and not yet discovered is extensive. Consequently, a burdensome amount of research would be required by one of ordinary skill in the art to practice the methods as instantly claimed.

(8) The relative skill of those in the art: The skill of one of ordinary skill in the art is relatively high, i.e., Ph.D. and M.D. level technology.

In the instant case, an impermissible burden of undue experimentation is necessary to determine which ACE inhibitors, angiotensin II receptor antagonists, or combinations thereof are effective in reducing the visible signs of fine lines on the skin or treating wrinkles. An exhaustive study would have to be conducted for each inhibitor, antagonist, or combinations thereof, possibly several more times with each study under slightly different conditions. *Genetech,* 108 F.3d at 1366, states that "a patent is not a hunting license. It is not a reward for a search, but compensation for a successful conclusion" and "[p]atent protection is granted in return for an enabling disclosure of an invention, not vague intimations of general ideas that may or may not be workable."

For the above reasons and analysis of the undue experimentation factors, a person skilled in the art would have to engage in undue experimentation to practice the methods of the instant claims with no assurance of success.

Claim Rejections - 35 USC § 103

11. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* v. *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

12. Claims 1, 3, 4, 11-20, 23, 27, and 28 are rejected under 35 U.S.C. 103(a) as being unpatentable over Alert et al. (US 5,728,373 – cited on IDS) in view of Chatterjee et al. (US 5,118,707).

Alert et al. teach cosmetic and dermatologic light protection formulations containing thiols and/or thiol derivatives wherein a preferred thiol is captopril (see abstract; column 3, lines 30-39) and wherein the formulations are suitable for the treatment of UV-induced skin damage (see column 2, lines 43-47). Alert et al. further teach a method for protecting the skin from UVA and UVB radiation comprising applying an adequate of the cosmetic or dermatological formulation to the skin, i.e. topical administration as claimed in the instant claims 1 and 18 (see column 10, lines 1-7). Alert et al. teach the cosmetic formulations can comprise cosmetic auxiliaries (i.e. carrier components) that are usually found in said formulations as claimed in the instant claim 12, and can be formulation into a lotion as claimed in the instant claim 13 (see column 6, line 53 to column 7, line 14). Alert et al. further teach the thiols or thiol derivatives (i.e. captopril) are preferably present in cosmetic and/or dermatological formulations in 0.01% by weight to 10% by weight (i.e. 100 mg/kg to 100,000 mg/kg), overlapping with the ranges as claimed in the instant claims 11 and 20 (see column 6, lines 26-35). In regards to claim 14, "repeatedly performing said contacting over an extended period of time" is broadly interpreted as applying a composition without rinsing it off. Thus, the application of the composition as taught by Alert et al. without rinsing the composition is considered to be application for an extended period of time.

Alert et al. do not explicitly teach reducing the visible signs of fine lines on the skin or the treatment of wrinkles by applying the captopril compositions to an individual in need thereof. Alert et al. do not explicitly teach the compositions are applied at least once daily as claimed in the instant claim 19.

Chatterjee et al. teach that photo damage (i.e. UV-induced skin damage) is a predominate cause of skin wrinkling (see column 7, lines 11-12).

It would have been obvious to one of ordinary skill in the art at the time of the invention to treat skin wrinkling as taught by Chatterjee et al. using the cosmetic and dermatologic light protection formulations containing captopril useful for the treatment of UV-induced skin damage as taught by Alert et al. One of ordinary skill in the art would have been motivated to treat skin wrinkling as taught by Chatterjee et al. using the cosmetic and dermatologic light protection formulations containing captopril useful for the treatment of UV-induced skin damage as taught by Alert et al. to treat wrinkles caused by UV radiation. One of ordinary skill in the art would have had a reasonable expectation of success in treating wrinkles as taught by Chatterjee et al. using the cosmetic and dermatologic light protection formulations containing captopril useful for the treatment of UV-induced skin damage as taught by Alert et al. because photo damage is a predominant cause of skin wrinkling. Thus, one of ordinary skill in the art would reasonably expect UV-induced skin damage to include wrinkles.

In regards to claim 16, wrinkling caused by UV-induced damage is considered premature.

In regards to claim 19, optimization of application of the composition taught by Alert et al. to at least once daily is considered to be within the purview of the ordinary artisan.

Thus, the invention as a whole would have been *prima facie* obvious to one of ordinary skill in the art at the time of the invention.

Response to Arguments

13. Applicant's arguments filed 11/23/2010 are moot in view of the new/modified ground(s) of rejection presented *supra*. However, Applicant's arguments have been addressed in so much as they apply to the new/modified ground(s) of rejection.

Applicant argues that ACE inhibitors and angiotensin II receptor antagonists constitute well recognized classes of drugs and thus one of skill in the art would comprehend the meaning of the broad class of materials and be able to use the material for the claimed purpose. In response it is respectfully submitted that while that ACE inhibitors and angiotensin II receptor antagonists constitute well recognized classes of drugs, the test of enablement is whether one skilled in the art could make or use the claimed invention from the disclosures in the application coupled with information known in the art without undue experimentation. Undue experimentation is not based on a single factor, but is a conclusion reached by weighing many factors as described *supra*. As stated in the 5/25/2010 Office action, there is little evidence in the prior art that these compounds can be used for improving aspects of an individual's skin tone.

Further, the Applicant supplies no evidence that ACE inhibitors and angiotensin II receptor antagonists can be used for said purpose. Applicant also states that ACE and angiotensin II are known to be involved in triggering collagen synthesis, whereas teaching with the prior art suggest that aging skin is associated with the reduction collagen. Thus, it is the Examiner's position that the treatment of the skin with said compositions for reducing the visible signs of fines on the skins and treating wrinkles would require undue experimentation.

Applicant further argues that Alert et al. do not teach the reduction or removal or treatment of existing wrinkles or visible signs of fine lines on the skin. In response it is respectfully submitted that Alert et al. teach the treatment of UV-induced skin damage (see column 2, lines 43-47). Further, Chatterjee et al. teach that photo damage is a predominant cause of skin wrinkling. Thus, it can reasonably be expected that an individual with UV-induced skin damage has skin wrinkling and that by treating UV-induced skin damage, skin wrinkling is treated.

Applicant further argues that aging of the skin, such as for example fine lines or wrinkling, is not necessarily an exhibition of skin damage caused by UV radiation. In response is respectfully submitted that Chatterjee et al. teach that photo damage is a predominant cause of skin wrinkling. The treatment of wrinkles associated with UV-induced skin damage are encompassed by the instant claims.

Thus, for these reasons, Applicant's arguments are found unpersuasive.

Conclusion

No claims are allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Correspondence

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jody L. Karol whose telephone number is (571)270-3283. The examiner can normally be reached on 8:30 am - 5:00 pm Mon-Fri EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreeni Padmanabhan can be reached on (571) 272-0629. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

/Jody L. Karol/

Examiner, Art Unit 1627

/Yong S. Chong/
Primary Examiner, Art Unit 1627